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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/811,283	03/15/2001	Todd J. A. Ewing	CAMIP005	2694

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EXAMINER
KENEDY, ANDREW A

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/811,283	EWING ET AL.	
	Examiner	Art Unit	
	Andrew A. Kenedy	1631	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) *21-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-53* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (Claims 1-20) in the response dated November 19, 2003, is acknowledged.

Claims 21-53 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the response of November 19, 2003.

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Applicants have not clearly stated the relationship between applications in the first sentence of the specification

Drawings

Applicant is advised that the instant application was incomplete as filed. Figure 9 was not submitted with the originally filed application papers. OIPE failed to send applicant a Notice of Omitted Items. The application is entitled to a filing date as the originally filed application

papers contained a written description and at least one claim. Applicant is required to do one of the following (see MPEP 601.01(g)):

> A) accept the application, as filed, without all of the drawing figure(s) referred to in the specification;
>
> (B) file any omitted drawing figure(s) with an oath or declaration in compliance with 37 CFR 1.63 and 37 CFR 1.64 referring to the omitted drawing figure(s) and a petition under 37 CFR 1.182 with the petition fee set forth in 37 CFR 1.17(h), requesting the date of submission of the omitted drawing figure(s) as the application filing date; or
>
> (C) file a petition under 37 CFR 1.53(e) with the petition fee set forth in 37 CFR 1.17(h) alleging that the drawing figure(s) indicated as omitted was in fact deposited with the USPTO with the application papers, including any and all evidence supporting the allegation. See MPEP § 503. The petition fee will be refunded if it is determined that the drawing figure(s) was in fact received by the USPTO with the application papers deposited on filing.
>
> If applicant is willing to accept the application, as filed, without all of the drawing figure(s) referred to in the application (item A above), applicant is required to submit (1) an amendment to the specification canceling all references to the omitted drawing figure(s) including any reference numerals shown only in the omitted drawing figure(s), (2) a separate letter renumbering the drawing figure(s) submitted on filing consecutively, accompanied by a copy of drawing figure(s) showing the proposed changes in red ink, and (3) a further amendment to the specification correcting references to drawing figure(s) to correspond with the relabeled drawing figure(s), both in the brief and detailed descriptions of the drawings. The amendment and the separate letter should be submitted in response to the Office action.
>
> Any petition filed in accordance with item B or C above should be filed with the TC. The TC will match the petition with the application file and forward the application file with the petition to the Office of Petitions, along with a brief explanation as to the drawing figure(s) that has been omitted on filing, for consideration of the petition in due course.

In view of the submission of a new Figure 9 (see submission on 6/26/01), it appears that applicant recognized that Figure 9 had been omitted; however, applicant failed to correct the omission as set forth above. Until the filing date issue has been resolved, submission of this new Figure 9 will not be addressed.

Claim Rejections - 35 USC § 112

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 requires for each identified reactive site: obtaining a lability value, and then characterizing the reactive site in terms of values for a plurality of chemical structural descriptors, and then using the lability values and chemical structural descriptor values to obtain an expression for lability that sums the contributions from each of the chemical structural descriptors. It is unclear how the lability values are obtained prior to and separately from the chemical structural descriptor values.

Furthermore, the claim requires obtaining an expression for lability that sums the contributions from each of the chemical structural descriptors, while no mention is made of how the expression for lability incorporates the individual lability values obtained initially. This is made more confusing because these steps are in conflict with the method outlined on page 20, lines 17-30 of the specification where, for each identified reactive site, the method steps include: identifying values for a plurality of chemical structural descriptors for the reactive site, and then calculating a lability value for the reactive site by summing terms of an expression wherein the terms include or are derived from the chemical structural descriptors. This second method clearly indicates that an individual lability value is derived by summing the chemical structural

descriptor values, which is in conflict with the method of Claim 1, where the lability values appear to be derived separately and independently from the chemical structural descriptor values.

It is therefore unclear how the individual lability values are derived and how the final expression for lability incorporates those values to produce a model of lability as in Claim 1.

Claims 1-10 require "identifying one or more reactive sites pertinent to the model." Applicants disclose a list examples of chemical bonds that may undergo oxidation and be analyzed by the instant invention (specification pg. 14, lines 19-27), however, this list includes many covalent bonds that are common and plentiful within organic molecules, so that overall no guidance is actually provided for identifying authentic reactive sites. Furthermore, no guidance or positive active steps are provided for identifying reactive sites that may undergo other types of chemical reactions, such as reduction, halogenation, sulfonation, etc., which may be pertinent to the model. One of ordinary skill in the art would not know how to identify reactive sites pertinent to the model without additional guidance or method steps.

Claims 11-20 require "identifying a reactive site on the chemical compound." Applicants disclose a list examples of chemical bonds that may undergo oxidation and be analyzed by the instant invention (specification pg. 14, lines 19-27), however, this list includes many covalent bonds that are common and plentiful within organic molecules, so that overall no guidance is actually provided for identifying authentic reactive sites. Furthermore, no guidance or positive active steps are provided for identifying reactive sites that may undergo other types of chemical reactions, such as reduction, halogenation, sulfonation, etc., which may be pertinent to the

model. One of ordinary skill in the art would not know how to identify reactive sites that could be used with applicants' instant invention to provide accurate predictions of lability.

Claims 1 and 11 require obtaining an expression of lability using lability values and/or structural chemical descriptor values. Applicants disclose an expression for activation energy of a reaction site that contains a summation of individual terms, each term consisting of the product of one unspecified coefficient and one unspecified variable (pg. 19, paragraph 3 of the specification). Applicants provide no examples or demonstration of what values are required to be input into the expression in order to produce a valid and reliable prediction of lability. It would appear that using values for chemical structural descriptors as required in Claim 1 and Claim 11, such as values for a partial charge on an atom or group at the reactive site and a geometric characterization of the reactive site, would not be appropriate values to be utilized in an expression that computes activation energy. One of ordinary skill in the art would not know how to use values for partial charge of an atom and geometric characterization of a reactive site in the expression for activation energy disclosed by the applicant. In the absence of any working examples, without guidance, and without positive active steps, it would not be possible or obvious for someone of ordinary skill in the art to carry out the applicants' instant invention as disclosed.

Claims 1 and 11 require obtaining an expression for lability and calculating a lability value, respectively. Applicants only provide an expression for calculating a lability value comprising activation energy. One of ordinary skill in the art would not know how to obtain an

expression for lability or calculate a lability value for reactivities such as ionization potential or delta enthalpy of formation using applicants' instant invention without guidance, formulas, or specific positive active steps.

Claims 5 and 17 require calculating a lability value comprising calculating activation energy, ionization potential, and delta enthalpy of formation. Applicants only disclose an expression for calculating activation energy. One of ordinary skill in the art would not know how to use the applicants' instant invention to calculate ionization potential or delta enthalpy of formation without guidance, formulas, or specific positive active steps.

Claim 20 requires "modifying said lability values to account for one or more particular reaction characteristics of one or more cytochrome P450 enzymes." The compound calcium carbonate is not a substrate for P450 enzymes. Therefore, one of ordinary skill in the art would not know how to modify a lability value for calcium carbonate, by accounting for one or more particular reaction characteristics of one or more cytochrome P450 enzymes. In fact, it appears that applicants have not provided any guidance, formulas, positive active steps, or examples to enable one of ordinary skill in the art to use the reaction characteristics of any cytochrome P450 enzyme to modify the lability value of any compound encompassed by applicants' invention.

Claims 1-10, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 requires "identifying one or more reactive sites pertinent to the model." The term "pertinent" is indefinite as to what types of reactive sites should be identified, thereby rendering the scope of the invention uncertain.

Claim 1 is drawn to "a method of producing a model that predicts the lability of reactive sites on a chemical compound." The term "model" is indefinite as to whether the method is supposed to produce a list of data values, a mathematical expression, an interactive three-dimensional animation displayed on a computer, etc., thereby rendering the scope of the invention uncertain.

Furthermore, it is unclear at what step a model is produced. The steps recited do not produce a model, but rather "an expression for lability" in the final step (d). As such, the steps are inconsistent with the preamble goal.

In Claim 1, applicants use the phrase "trustworthy source or technique" which is indefinite. Applicants do not disclose any definition, decision criteria, or examples of a trustworthy source, so that it would be unclear to one of ordinary skill in the art what would qualify as a trustworthy source. While applicants do disclose examples of what may comprise a trustworthy technique, criteria for determining whether other techniques are trustworthy are not disclosed, and therefore one of ordinary skill in the art would not know whether or not other techniques could be used with applicants' invention to produce a meaningful result.

With respect to Claims 5 and 6, the term "trustworthy technique" is indefinite. Applicants use the term "trustworthy technique" in open-type phrases claiming what may comprise a "trustworthy technique". However, disclosure of criteria for determining whether other techniques are trustworthy is not provided, and therefore one of ordinary skill in the art would not know whether or not other techniques could be used with applicants' invention to produce a meaningful result.

With respect to Claim 7, it is unclear as to what is meant by the phrase "fragment-based descriptors." This terminology does not appear to have an art understood meaning.

With respect to Claims 7 and 8, applicants do not disclose a definition, description, or example of what constitutes either the "aliphatic hydrogen abstraction model" of Claim 7, or the "aromatic oxidation model of Claim 8. It is therefore unclear what would be required to meet the limitations of Claims 7 and 8.

Claim 20 requires "modifying said lability values to account for one or more particular reaction characteristics of one or more cytochrome P450 enzymes." The term "modifying" is indefinite in that it gives no indication of how the lability value is to be adjusted. The phrase "one or more particular reaction characteristics" is indefinite because it does not clearly indicate what the reaction characteristics are or what values or information could be derived from them so as to then modify a numerical lability value, thereby rendering the scope of the invention uncertain.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 6, 9-11, 14, 15, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Karickhoff et al. (IDS document No. C1).

With respect to Claim1, Karickhoff et al. teaches a method for producing a model that predicts the reactivity of reaction sites (lability of reactive sites) of a chemical compound (see at least the abstract; and Fig. 1), the method comprising: (a) obtaining structural representations for a training set of chemical compounds (see at least the abstract; and pg. 1413, col. 2, paragraph 1 entitled *Model Parameterization*); (b) for each compound, identifying one or more reaction sites (reactive sites) pertinent to the model (see at least pg. 1407, col. 2, paragraph 1 entitled *Structure Classification*); (c) for each reactive site, obtaining (i) a reactivity value (lability value) from directly measured data (a trustworthy source) (see at least pg. 1408, col. 1, paragraph 1; and Table 1), and (ii) characterizing the site in terms of values for a plurality of chemical structural descriptors including at least two of an atom type at the reaction site, atom types at neighboring positions to the reactive site, a partial charge on an atom or group at the reactive site, and a geometric characterization of the reaction site (see at least pg. 1407, col. 2, paragraph 1; pg. 1408, col. 1 - 2; Table 1; pg. 1409, col. 1; pg. 1414, col. 2, bridge paragraph; and Fig. 3); and (d)

for all reaction sites, obtaining an expression for reactivity (lability) that sums the contributions from each of the chemical structural descriptors (see at least Fig. 2).

With respect to Claim 5, Karickhoff et al. teaches that obtaining a reactivity value (lability value) comprises calculating a delta Enthalpy of formation for the intermediate radical formed at the reactive site (see at least pg. 1408, col. 1).

With respect to Claim 6, Karickhoff et al. teaches that the technique used to provide reactivity values employs a description of quantum effects and quantum contributions (quantum mechanical representation) of the chemical compounds of the training set (see at least pg. 1407, col. 1, paragraph 1).

With respect to claims 9 and 10, Karickhoff et al. teaches that obtaining an expression for lability by employing a nonlinear, least-squares matrix method (partial least squares regression) to process a set of designated training data and provide an optimized set of model parameters for reactivity of reaction sites on a compound.

With respect to Claim 11, Karickhoff et al. teaches a method on a computing device for predicting reactivity (labilities) of reaction sites (reactive sites) on a chemical compound (see at least the abstract; and Fig. 1), the method comprising: (a) identifying a reaction site (reactive site) on the chemical compound (see at least pg. 1407, col. 2, paragraph 1 entitled *Structure Classification*); (b) identifying values for a plurality of chemical structural descriptors including

at least one of an atom type at the reaction site, atom types at neighboring positions to the reactive site, a partial charge on an atom or group at the reactive site, and a geometric characterization of the reaction site (see at least pg. 1407, col. 2, paragraph 1; pg. 1408, col. 1 - 2; Table 1; pg. 1409, col. 1; pg. 1414, col. 2, bridge paragraph; and Fig. 3); (c) calculating a reactivity parameter (lability value) for the reactive site, by summing terms of an expression, wherein the terms include or are derived from individual ones of the chemical structural descriptors (see at least Fig. 2); (d) repeating steps (a)-(c) for more additional reactive sites of the chemical compound (see at least pg. 1412, col. 2, paragraph 1 entitled *Model Execution*; pg. 1413, col. 1, paragraph 1); and (e) outputting the reactivity values (lability values) calculated at (c) for the reactive sites on the chemical compound (see pg. 1413, col. 1, paragraphs 1-2; and pg. 1413, col. 2, bridge paragraph).

With respect to Claim 14, Karickhoff et al. teaches that the chemical structural descriptors are selected from the group consisting of an atom type at the reaction site, atom types at neighboring positions to the reactive site, a partial charge on an atom or group at the reactive site, and a geometric characterization of the reaction site (see at least pg. 1407, col. 2, paragraph 1; pg. 1408, col. 1 - 2; Table 1; pg. 1409, col. 1; pg. 1414, col. 2, bridge paragraph; and Fig. 3).

With respect to Claim 15, Karickhoff et al. teaches a linear expression for reactivity (a lability value) shown in equation 5 (see pg. 1409, col. 1, paragraph 2) that has a defined coefficient, $1/D_c$, for each chemical structural descriptor in the expression.

With respect to Claim 18, Karickhoff et al. teaches simultaneously displaying the reactivity parameters (lability values) calculated for all reactive sites (see at least Fig. 1; Fig. 3; and pg. 1413, col. 2, bridge paragraph).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Karickhoff et al. (IDS document No. C1) in view of Jones et al. (IDS document No. 3I).

Karickhoff et al. is applied as above. Karickhoff et al. does not teach that the structural representations are three-dimensional depictions including at least bond lengths and bond angles

Jones et al. teaches a method of predicting the reactivity of nicotine enantiomers with cytochrome P450 enzyme, where the structural representations used in making the prediction include bond lengths and bond angles (see at least the abstract; Fig. 3; and pg. 386, col. 1, paragraph 2).

It would have been obvious for one of ordinary skill in the art to combine the teachings of Jones et al. with the method of Karickhoff et al., since Jones et al. teaches that differences in the three-dimensional structure of a compound can have significant effects on reactivity of that compound (see at least the abstract; pg. 384, col. 1, paragraphs 1-3; and Table IV).

Claims 3 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karickhoff et al. (IDS document No. C1) in view of Yin et al. (IDS document No. 6L).

Karickhoff et al. is applied as above. Karickhoff et al. does not teach the particular limitation of predicting reactivity (lability) for oxidation reactions.

Yin et al. teaches a computational model for predicting oxidative reactivity of compounds where the oxidation reaction is an aliphatic hydrogen atom abstraction (see at least the abstract).

It would have been obvious for one of ordinary skill in the art to combine the teachings of Yin et al. with the method of Karickhoff et al. to predict the reactivity of an oxidation reaction such as hydrogen abstraction involving the step of identifying reactive sites where the oxidation reaction can occur in the training set of chemical compounds, since Yin et al. teaches that use of a computational model for predicting the rate of hydrogen-atom abstraction by cytochrome P450 enzymes "can be used as a tool in the design of safer chemicals...The design of chemicals with the lowest possible toxicity would decrease the damage to the environment; decrease the costs of production, health care, and site remediation; and increase the safety in the workplace" (See the abstract; and col. 1, paragraph 1).

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Karickhoff et al. (IDS document No. C1) in view of Yin et al. (IDS document No. 6L).

Karickhoff et al. is applied as above. Karickhoff et al. teaches that the model employs parameters for appended structures, reaction centers, and substituents of the compound

(fragment-based descriptors) (see at least pg. 1409, col. 1, paragraph 1), but does not teach that the model is an aliphatic hydrogen abstraction model.

Yin et al. teaches an aliphatic hydrogen abstraction model (see at the abstract).

It would have been obvious for one of ordinary skill in the art to combine the teachings of Yin et al. with the method of Karickhoff et al. to provide an aliphatic hydrogen abstraction model wherein the descriptors comprise 'fragment-based descriptors', since Yin et al. teaches that use of a computational model for predicting the rate of hydrogen-atom abstraction by cytochrome P450 enzymes "can be used as a tool in the design of safer chemicals...The design of chemicals with the lowest possible toxicity would decrease the damage to the environment; decrease the costs of production, health care, and site remediation; and increase the safety in the workplace" (See the abstract; and col. 1, paragraph 1).

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Karickhoff et al. (IDS document No. C1) in view of Jones et al. (IDS document No. 3H).

Karickhoff et al. is applied as above. Karickhoff et al. does not teach an aromatic oxidation model, wherein the descriptors comprise geometry-based descriptors.

Jones et al. teaches an aromatic oxidation model for determining the lability of a reactive site on benzo[a]pyrene to oxidation by P450 enzymes, wherein the descriptors comprise geometry-based descriptors (see at least the abstract; Scheme 1; Fig. 1; pg. 6957, col. 2, paragraph 2-3; and pg. 6959, col. 2, bridge paragraph).

It would have been obvious for one of ordinary skill in the art to combine the teachings of Jones et al. with the method of Karickhoff et al. to provide a method for predicting the lability of

reactive sites on a molecule to aromatic oxidation using geometry-based descriptors, since Jones et al. teaches that aromatic oxidation of the procarcinogen benzo[a]pyrene results in the production of "the most potent diol epoxide carcinogen in man" (see pg. 6956, col. 2, bridge paragraph; and the abstract).

Claims 12, 13, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karickhoff et al. (IDS document No. C1) in view of Yin et al. (IDS document No. 6L).

Karickhoff et al. is applied as above. Karickhoff et al. does not teach the particular limitation of the reactive site being susceptible to oxidation reactions, wherein the chemical structural descriptors are specific for the oxidation reaction to which the reactive site is susceptible, and wherein the expression for reactivity (lability) is specific for the oxidation reaction to which the reactive site is susceptible.

Yin et al. teaches a computational model for predicting oxidative reactivity of compounds where the oxidation reaction is an aliphatic hydrogen atom abstraction and the chemical structural descriptors and expression for lability are specific for the reaction type (see at least the abstract; pg. 11076, col. 2, paragraph 1; and Table 2).

It would have been obvious for one of ordinary skill in the art to combine the teachings of Yin et al. with the method of Karickhoff et al. to provide a computational model for predicting oxidative reactivity of compounds where the oxidation reaction is an aliphatic hydrogen atom abstraction wherein the chemical structural descriptors and expression for reactivity (lability) are specific for the type of oxidation reaction, since Yin et al. teaches that use of a computational model for predicting the rate of hydrogen-atom abstraction by cytochrome P450 enzymes "can

be used as a tool in the design of safer chemicals...The design of chemicals with the lowest possible toxicity would decrease the damage to the environment; decrease the costs of production, health care, and site remediation; and increase the safety in the workplace" (See the abstract; and col. 1, paragraph 1).

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Karickhoff et al. (IDS document No. C1) in view of Yin et al. (IDS document No. 6L).

Karickhoff et al. is applied as above. Karickhoff et al. teaches that the reactivity parameter (lability value) represents a delta enthalpy of formation of the transition state (intermediate radical) at the reaction site (see pg. 1408, col. 1, bridge paragraph and paragraph 1). Karickhoff et al. does not teach that the reaction is an oxidative reaction, or that the reactivity value can alternatively be an activation energy of the oxidative reaction.

Yin et al. teaches a computational model for predicting oxidative reactivity of compounds (see at least the abstract). Yin et al. also teaches that the reactivity value for oxidation reaction can be an activation energy (see at least the abstract; and pg. 11076, col. 2, paragraph 1).

It would have been obvious for one of ordinary skill in the art to combine the teachings of Yin et al. with the method of Karickhoff et al. to provide a computational model for predicting oxidative reactivity of compounds where the reactivity parameter (lability value) can represent a delta enthalpy of formation of the transition state (intermediate radical) at the reaction site or an activation energy of the oxidation reaction, since Yin et al. teaches that use of a computational model for predicting the rate of hydrogen-atom abstraction by cytochrome P450 enzymes "can

be used as a tool in the design of safer chemicals...The design of chemicals with the lowest possible toxicity would decrease the damage to the environment; decrease the costs of production, health care, and site remediation; and increase the safety in the workplace" (See the abstract; and col. 1, paragraph 1).

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Karickhoff et al. (IDS document No. C1) in view of Subramaniam et al. (IDS document No. A2).

Karickhoff et al. is applied as above. Karickhoff et al. does not teach that outputting the calculated reactivity parameters (lability values) comprises sending the values to a remote network site from which a request to predict the values has originated.

Subramaniam et al. teaches a computer system and method for sending biological data values, in response to a user query or command request, to a remote network site from which a user request originated (see at least the abstract).

It would have been obvious for one of ordinary skill in the art to combine the teachings of Subramaniam et al. with the method of Karickhoff et al. to provide a method that outputs the calculated reactivity parameters (lability values) comprising sending the values to a remote network site from which a request to predict the values has originated, since Subramaniam et al. teaches that "there is a need for global communication of information in molecular biology...the nature of bench work in the fields of molecular and structural biology [has] chang[ed], becoming increasingly dependent upon information retrieval" (see col. 2, lines 4-6; and col. 1, lines 50-53).

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Karickhoff et al. (IDS document No. C1) in view of Jones et al. (IDS document No. 3H).

Karickhoff et al. is applied as above. Karickhoff et al. does not teach correcting the reactivity parameters (lability values) to account for one or more particular reaction characteristics of one or more cytochrome P450 enzymes.

Jones et al. teaches an aromatic oxidation model for determining the lability of a reactive site on benzo[a]pyrene toward oxidation by P450 enzymes, wherein they explain that in most P450 catalyzed reactions, the various P450 enzymes often differ in both regioselectivity and stereoselectivity, which can effect the reaction outcome of a reactive site on a substrate compound (see at least the abstract).

It would have been obvious for one of ordinary skill in the art to combine the teachings of Jones et al. with the method of Karickhoff et al. to provide a method for predicting the lability of reactive sites on a molecule to aromatic oxidation using geometry-based descriptors, since Jones et al. teaches that aromatic oxidation of the procarcinogen benzo[a]pyrene results in the production of "the most potent diol epoxide carcinogen in man" (see pg. 6956, col. 2, bridge paragraph; and the abstract).

Made of Record

Prior Art made of record which discloses various aspects of applicants' instant invention but was not relied upon:

Applicants' IDS documents: Korzekwa et al. (*Pharmacogenetics*, 1993), Korzekwa et al. (*Journal of the American Chemical Society*, 1990), Wislocki et al. (*Enzymatic Basis of Detoxification, Vol. 1*, Chapter 7, 1980).

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew A. Kenedy whose telephone number is (571)-272-0574. The examiner can normally be reached on Monday-Friday 9:00am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)-272-0722. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-0549.

A.A.K.
February 2, 2004

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
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